REMARKS

Claim Amendments

Claim 28 has been amended to recite a method involving the use of a nucleic acid probe that has a probe linker at each of the two ends of the probe unit. Teaching for such probe configuration can be found on page 27, lines 14-23; page 28, lines 9-22; and Figure 3.

Claim 29 has been amended to recite a method involving the use of a nucleic acid probe comprising two overlapping oligonucleotide. The first oligonucleotide comprises a sequence complementary to the single-stranded target nucleotide sequence flanked by a first probe linker on one end and an overlap linker on the other end, wherein said overlap linker is hybridized to a second oligonucleotide comprising a second probe linker. Teaching for such probe configuration can be found on page 27, lines 24 to page 28, line 4; and Figure 3A.

Claims 30-31 have been amended to recite a reporter comprising a labeled, double-stranded polynucleotide sequence linked on one or both ends to a reporter linker that comprises short single-stranded polynucleotide. Teaching for such reporter configuration can be found on page 29, lines 13-18.

Claim 32 has been amended to recite a reporter array formed by two or more reporters linked end-to-end via reporter linkers. Teaching for such reporter array can be found on page 29, lines 19-26.

Claim 33 has been amended to recite using a terminator oligonucleotide to terminate a reporter array. Teaching for such terminator can be found on page 8, lines 23-25; page 33, lines 15-20; and Figures 4B-C, 5B.

Claim 34 has been amended to recite a reporter array comprising successive layers of type I and type II reporters, wherein the first and second reporter linker of a type I reporter is hybridized respectively to the second reporter linker of a type II reporter and to the first reporter linker of another type II reporter, except the first reporter linker of the type I reporter in the first layer of reporter is hybridized to a probe linker of a probe.

Teaching for such reporter array can be found on page 66, lines 19-21; page 67, line 27 to page 68, line 2; and Figure 7B.

Claim 35 has been amended to recite using a multi-linking unit comprising (i) a sequence that hybridizes to the probe linker and (ii) two or more sequences that hybridize to the reporter linker of the reporter. Teaching for such multi-linking unit can be found on page 32, lines 21-29; and Figure 14.

Claim 38 has been amended to recite a method of detecting a target nucleotide sequence and providing a circular enclosure of the target sequence (see Figure 17). The method involves the use of a first probe, a second probe, a first ring subunit, a second ring subunit and a reversing oligonucleotide (oligonucleotides A-E of Figure 17A). Hybridization among these five oligonucleotides forms a circular enclosure around the target sequence (see Figure 17B). The presence of target sequence is detected by reporter sequences which are linked to the reporter linker sequences extending from the circular enclosure (Figure 17B). Teaching for the above method can be found on page 6, lines 14-22; page 35, line 23 to page 36, line 4; and Examples 6-7.

Claim 39 has been amended to recite a method of simultaneously detecting a target sequence on both a sense and anti-sense strand of DNA (see Figure 19). This method involves the use of probes, ring subunits and reversing oligonucleotide as described in Figure 17A. Hybridization among one set of these oligonucleotides forms a circular enclosure around the target sequence on the sense strand, whereas hybridization among another set of these oligonucleotides forms a circular enclosure around the target sequence on the anti-sense strand (see Figure 19A). The presence of sense and anti-sense strand target sequences can then be detected by two different kind of reporter sequences which are linked to the reporter linker sequences extending from the circular enclosures (Figure 19B). Teaching for the method of claim 39 can be found on page 6, lines 22-27; page 36, lines 4-8; and Example 8.

Claim 58 is added to recite a method of detecting a target nucleotide sequence and providing a circular enclosure of the target sequence (see Figure 18). The method involves the use of a probe, a first ring subunit, a second ring subunit and a lock oligonucleotide (oligonucleotides A-D of Figure 18A). Hybridization among these

oligonucleotides forms a circular enclosure around the target sequence (see Figure 18B). The presence of target sequence is detected by reporter sequences which are linked to the reporter linker sequences extending from the circular enclosure (Figure 18B). Teaching for the above method can be found on page 6, lines 14-22; page 35, line 23 to page 36, line 4; and Examples 6-7.

Claim 59 is added to claim the overlap linker recited in claim 29 comprises one or more TA sequence to facilitate crosslinking during probe fabrication. Teaching for such overlap linker can be found on page 28, lines 4-8.

Claim 60 is added to claim the reporter linker recited in claim 30 comprises a carbon spacer segment. Teaching for such reporter linker (designated as Gene-Tag in the specification) with carbon spacer can be found on page 28, line 24 to page 29, line 7; page 30, line 27 to page 31, line 26; and Figure 4.

Claim 61 is added to claim the reporter linker recited in claim 30 comprises sequence selected from the group consisting of SEQ ID NO. 6, 10, 71, 76 and 81.

Applicant submits that these amended claims have not introduced any new matter to the application.

Rejections Under 35 USC §112, 2nd Paragraph

Claims 28-39 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Claim 28 is rejected for reciting vague and indefinite phrase. Claims 38-39 are rejected for reciting "ring-tail" and confusing method steps.

Applicant submits that the claims have been amended to delete indefinite phrases rejected by the examiner. Claims 38-39 have been amended as described above. Applicant submits that the claims have been amended to particularly point out and distinctly claim the subject matter of the invention. Accordingly, Applicant requests that the rejection of claims 28-39 under 35 U.S.C. §112, second paragraph, be withdrawn.

Rejections Under 35 USC §102

Claims 28-36 are rejected under 35 USC §102(e) as being anticipated by **Urdea** et al. (U.S. Patent 5,681,697). The examiner contends that **Urdea** teaches

hybridizing a single-stranded target nucleotide sequence with a nucleic acid probe where the nucleic acid probe comprises a central sequence complementary to the target sequence and further comprises a probe linker at one terminal end, said probe linker comprises a single-stranded nucleotide sequence that does not hybridize to the target sequence. This rejection is respectfully traversed.

Applicant submits that in contrast to **Urdea** et al., the present invention is drawn to a method of hybridizing a single-stranded target nucleotide sequence with a nucleic acid probe that comprises (i) a sequence complementary to the single-stranded target nucleotide sequence, and (ii) a probe linker at each of the two terminal ends of the probe. Hence, while **Urdea** teaches using a probe with only one terminal probe linker, the present invention claims a method of using a probe that has two terminal probe linkers, one at each of the two ends of the probe. A claim is anticipated only if each and every element as set forth in the claim is found in the cited prior art reference. The identical invention must be shown in as complete detail as is contained in the claim. Accordingly, since **Urdea** does not teach or suggest a method of using a probe with probe linkers at both ends of the probe, **Urdea** et al. do not anticipate the present invention.

The examiner contends that **Urdea** teaches a probe that comprises a first and second terminal probe linker (see Figure 16, where the LE has an X and Y region that hybridizes to the Amp1 probe). Applicant respectfully disagrees. Applicant submits that **Urdea** only teaches using a probe with one terminal probe linker. **Urdea** does not teach or suggest a method of using a probe with probe linkers at both ends of the probe as claimed herein. From column 10, line 61 to column 11, line 7, **Urdea** teaches:

> "Label extender molecules (LEs)", also referred to herein as "label extenders", contain regions of complementarity vis-à-vis the analyte polynucleotide and to the amplifier multimer.... Thus, label extender molecules are single-stranded polynucleotide chains having a first nucleic acid sequence L-1 complementary to a sequence of the analyte polynucleotide, and a second region having a multimer recognition sequence L-2 complementary to a segment M-1 of label probe, amplifier multimer or preamplifier.

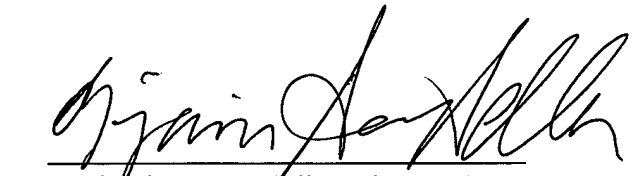
Thus, **Urdea** only teach a probe with only one terminal probe linker, i.e. a probe (LE) with a L-1 region complementary to target sequence and a L-2 region complementary to a label reporter or amplifier. This is consistent with what are shown in Figures 8, 11-13, and 15. Similarly, Figure 16 shows one LE probe with one terminal linker X and another LE probe with one terminal linker Y. The second vertical line connected to the end of LE probe in Figure 16 (which may be mistaken as a second terminal linker) is not labeled as terminal linker and is not hybridized to any label reporter or amplifier. In view of the teaching as a whole, Applicant submits that **Urdea** does not teach or suggest a probe with terminal linkers at both ends of the probe, and Figure 16 should not be taken as teaching LE probe having two terminal linkers at both ends of the probe.

Claims 29-34 and 35 are dependent from independent claim 28 which recites a method of using a probe with probe linkers at both ends of the probe. As discussed above, since **Urdea** does not teach or suggest a method of using a probe with probe linkers at both ends of the probe, **Urdea** does not teach or anticipate claims 29-33 and 35 of the present invention. Claim 36 has been canceled. Accordingly, Applicant respectfully request that the rejection of claims 28-35 under 35 USC §102(e) be withdrawn.

This is intended to be a complete response to the Office Action mailed October 28, 2004. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

Date: Feb 11, 2005



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